De novo biosynthesis of α-aminoadipate via multi-strategy metabolic engineering in Escherichia coli

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Abstract

As a non-protein amino acid, α-aminoadipate is used in the fields of medicine, chemical engineering, and others. In addition, α-aminoadipate is an important precursor for the synthesis of β-lactam antibiotics. In this study, we construct a biosynthesis pathway of α-aminoadipate in Escherichia coli using lysine as the precursor and produce α-aminoadipate using a microbial cell factory for the first time. In addition, we regulate the cell metabolism to improve the titer of α-aminoadipate via multi-strategy metabolic engineering. First, a novel synthetic pathway was constructed to realize the de novo synthesis of α-aminoadipate with the titers of 82 mg/L. Second, the key enzymes involved in enhancing precursor synthesis were overexpressed and the CO2 fixation process was introduced, and these led to 80% and 34% increases in the α-aminoadipate concentration, reaching 147 mg/L and 110 mg/L, respectively. Third, cofactor regulation was used to maintain the coupling balance of material and energy, with the intracellular α-aminoadipate concentration reaching 140 mg/L. Fourth, the weakening of the synthesis of acetic acid was used to strengthen the synthesis of α-aminoadipate, and this resulted in the enhancement of the α-aminoadipate concentration by 2.2 times, reaching 263 mg/L. Finally, combination optimization was used to promote the production of α-aminoadipate. The titers of α-aminoadipate reached 415 mg/L, which was 4 times higher than that of the parent strain. This study is the first to present the effective biosynthesis of α-aminoadipate in E. coli.

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